Generation of hepatic cell from placental stem cell for congenital metabolic disorders

Grant Award Details

Generation of hepatic cell from placental stem cell for congenital metabolic disorders

Grant Type: Early Translational III

Grant Number: TR3-05488

Project Objective: The goal of this DCF project is to demonstrate proof-of-concept that subsets of cells expressing high levels of certain individual hepatic enzymes (OTC, IDUA or BCKDHA) can be isolated from human amniotic epithelial cells (hAEC) and can demonstrate therapeutic efficacy after transplantation into murine models of congenital metabolic diseases caused by deficiencies in those enzymes.
OTC = ornithine transcarbamylase Disease = OTC
IDUA = alpha-L-iduronidase Disease = mucopolysaccharidosis type 1
BCKDHA = branched chain keto acid dehydrogenase Disease = Maple syrup urine disease
October 2015: This project is entering a 12-month NCE. I recommended at the time of the PAR for the NCE that Dr. Miki focus on a single disease model in order to get the most complete package of data possible with the remaining time and money, in order to best position himself for moving further in development. He has chosen to focus on OTC (biggest unmet need).

Investigator:

Name:	Toshio Miki
Institution:	University of Southern California
Type:	PI

Disease Focus: Liver Disease, Metabolic Disorders, Pediatrics

Human Stem Cell Use: Adult Stem Cell

Award Value: $1,750,375

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: Y4 / NCE

View Report

Grant Application Details

Application Title: Generation of hepatic cell from placental stem cell for congenital metabolic disorders

Public Abstract: Approximately 1 in 1,500 children has a congenital metabolic disorder. These inborn errors of metabolism are caused by deficiencies of different enzymes and result in accumulation of various substances inside cells. These substances affect the function of vital organs, and in many cases are lethal. Transplantation of cells that possess the particular deficient enzyme carries the potential to cure these diseases. Currently, a shortage of human liver cells for transplantation prohibits clinical use of this therapy. The human placenta contains cells that may acquire hepatic function. Following delivery of a baby, these cells can be collected from the placenta which is in most cases is treated as medical waste and discarded. The therapeutic potential of this cell type has been shown in animal models. We propose to first develop a method to separate these cells from non liver like cells, and secondly use these cells to treat multiple mouse models of human inborn errors of metabolism. We will also establish a clinically applicable small-scale preparatory Bio-banking system to provide immunotype-matched cells to patients affected by these diseases. These immunotype-matched cells can replace the missing enzyme function in patients who suffer from congenital liver metabolic disorders, and potentially will be cure the condition. Although this proposal focuses on the congenital liver metabolic disorders, success may lead to the use of these cells in other liver diseases.

Statement of Benefit to California: We propose to develop a technology to isolate and derive functional hepatic cells from discarded human placentae. The therapeutic cells will be utilized to treat congenital metabolic disorders. Current therapy for congenital metabolic disorders requires life-long treatment. It is easy to imagine how the economical burden afflicts the patients' families and society. If successful, immuotype matched hAEC-derived cell replacement therapy may completely cure some of the congenital metabolic disorders. The benefit of this new regenerative medicine will be tremendous not only for the patients' quality of life but also for our society. Although this proposal focuses on the congenital liver metabolic disorders, the target disease can potentially be extended to other liver diseases. This cell therapy would be the first cell therapy for liver disease and could benefit thousands of patients in California who suffer various liver diseases. Furthermore, once this therapeutic potential is demonstrated, a placenta collection system, placental stem cell banking system, and a stem cell-derived hepatic cell distribution system might be a novel industry or industries that could provide job opportunities to the citizens of California.